STUDY ON ROLE MAGNESIUM SULPHATE IN ATTENUATING SUCCINYLCHOLINE INDUCED FASCICULATION AND POST OPERATIVE MYALGIA

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IN

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BRANCH X

INSTITUTE OF ANAESTHESIOLOGY & CRITICAL CARE

MADRAS MEDICAL COLLEGE

CHENNAI- 600 003

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CERTIFICATE

This is to certify that the dissertation entitled, "**STUDY ON ROLE OF MAGNESIUM SULPAHTE IN ATTENUATING SUCCINYLCHOLINE INDUCED FASCICULATION AND POST OPERATIVE MYALGIA",**Submitted by Dr. K. ELAYAVENDHAN in partial fulfilment for the award of the degree of Doctor of Medicine in Anaesthesiology by the Tamilnadu Dr. M.G.R. Medical University, Chennai is a bonafide record of the work done by him in the INSTITUTE OF ANAESTHESIOLOGY & CRITICAL CARE, Madras Medical College, during the academic year 2011-2013.

R.M.VASANTHI,M.D.,D.A.,DNB.,
PROFESSOR AND DIRECTOR
INSTITUTE OF ANAESTHESIOLOGY & CRITICAL CARE
MADRAS MEDICAL COLLEGE
CHENNAI- 600003

DR.V.KANAGASABAI, M.D.,
DEAN
MADRAS MEDICAL COLLEGE
& GOVT.GENERAL HOSPITAL
CHENNAI-600003

DECLARATION

I, **Dr. K. ELAYAVENDHAN**, solemnly declare that this dissertation entitled **"STUDY ON ROLE OF MAGNESIUM IN ATTENUATING SUCCINYLCHOLINE INDUCED FASCICULATION AND POST OPERATIVE MYALGIA"** is a bonafide work done by me in the Institute of Anaesthesiology & critical care, Madras Medical College and Rajiv Gandhi Government General hospital, Chennai, during the period 2010-2013 under the able guidance of **Prof. *M. VASANTHI, MD., DA., DNB.,*** Director, Institute of anaesthesiology & critical care, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai – 3 and submitted to **The Tamilnadu Dr. MGR Medical University,** Guindy, Chennai – 32, in the partial fulfillment of the requirements for the award of the degree of MD Anaesthesiology (Branch X).

Place:

Date:

(Dr. K. ELAYAVENDHAN)

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CONTENTS

INTRODUCTION

The neuromuscular transmission has fascinated the anaesthesiologist ever since the usage of curare as a muscle relaxant in anaesthesia practise.

CLAUDE BERNARD in his series of the effects of curare on nerve muscle preparations suggested the electrical transmission in the nerve and the presence of chemical molecule which is critical for the transfer of information between nerve and muscle.

VULPAIN suggested the presence of a junction between terminal nerve and muscle and his suggestions were later confirmed from later studies.

LANGLEY in 1905 explained and proved that a chemical molecule is present between nerve and the muscle to initiate a muscle contraction.

Succinylcholine is still one of the most commonly used muscle relaxant in clinical practice since its introduction by Theslaff and colleagues. Though being the fastest and short acting muscle relaxant it is not free of complications.

Fasciculation is an inevitable feature of Succinylcholine. It is because of this Succinylcholine induced muscle fasciculation that causes hyperkalemia, increased intra ocular pressure, increased intra cranial pressure, increased intra gastric pressure and myalgia. So by blunting this fasciculation we can avoid all the above mentioned complications of Succinylcholine. Several drugs has been used to blunt this Succinylcholine induced muscle fasciculation. They are Rocuronium, Atracurium, Ketorolac, Lignocaine, Diazepam, Magnesium sulphate, Thiopentone, Diclofenac, small dose of Succinylcholine itself, Vecuronium, Pancuronium, and D-Tubocurare. In our study we used Magnesium sulphate at a dose of 40mg/kg to blunt this Succinylcholine induced muscle fasciculation. We used Propofol as an induction agent in our study because it has been shown in various studies that Propofol is a better agent than Thiopentone in reducing Succinylcholine induced muscle fasciculation.

AIM OF THE STUDY

The aim of our study is to study the role of Magnesium sulphate in attenuating Succinylcholine induced muscle fasciculation and Succinylcholine induced post operative myalgia. In our study we have compared the effect of Magnesium sulphate with Propofol and Propofol alone on Succinylcholine induced fasciculation and myalgia.

ANATOMY OF NEUROMUSCULAR JUNCTION

The neuromuscular junction is formed where a motor nerve travels as large myelinated axon and meets the muscle fibre.

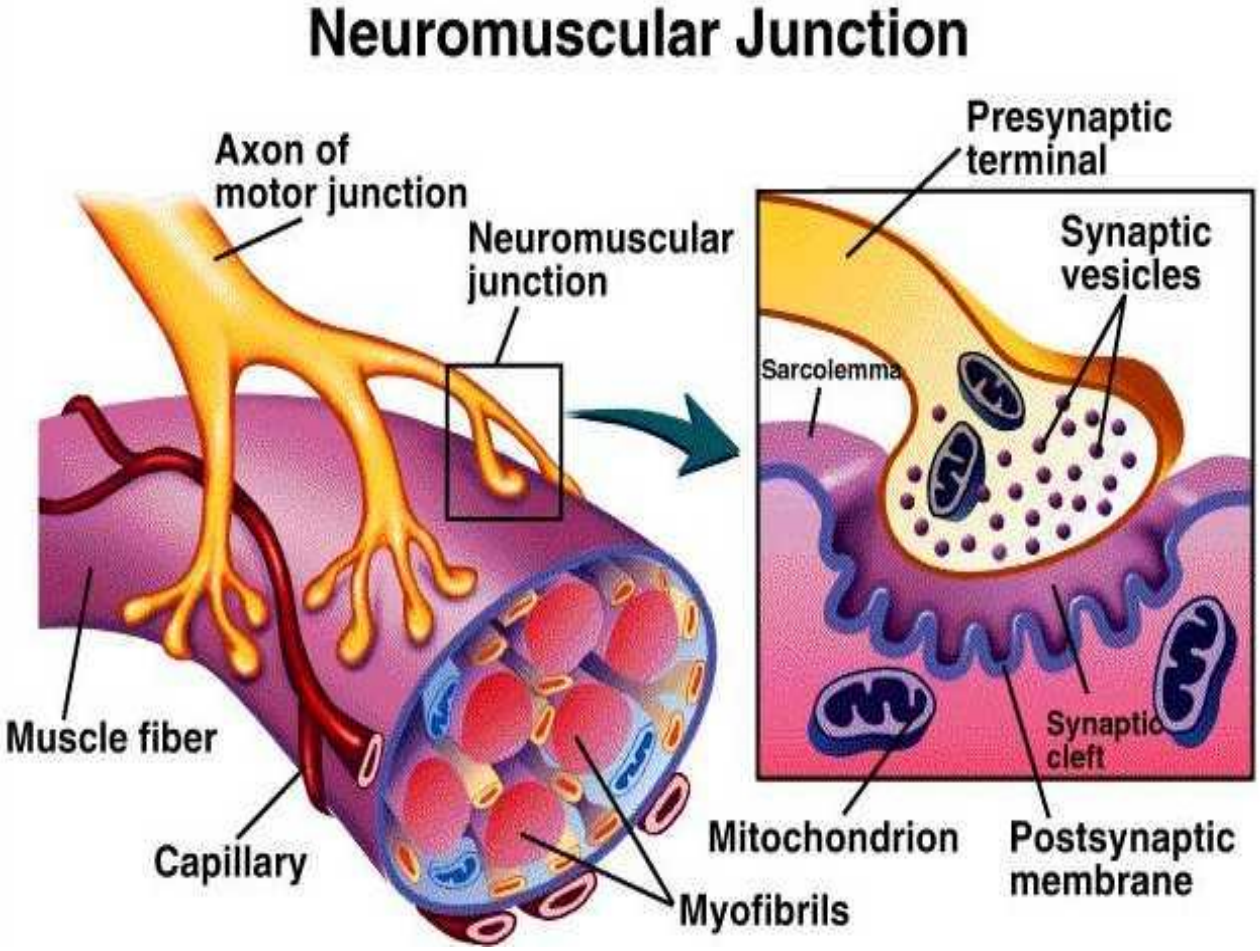

Fig 3.1. NEUROMUSCULAR JUNCTION

ANATOMY OF NEUROMUSCULAR JUNCTION

- The neuromuscular junction is specialized on the nerve side and on the muscle side to transmit and receive chemical messages.
- Each motor nerve travels from the ventral horn of spinal cord to the neuromuscular junction as a large myelinated axon.
- As it approaches the muscle it branches repeatedly to contact many muscle cells and gather them into a functional group known as **MOTOR UNIT.**
- As the terminal reaches the muscle fiber, it loses its myelin sheath, forms a spray of terminal branches against the muscle surface and is covered by Schwann cells.

THE NEUROMUSCULAR JUNCTION consists of three distinct parts:

- **PRE SYNAPTIC ZONE**
- **SYNAPTIC CLEFT**
- **POST SYNAPTIC ZONE**

These three components jointly form the neuromuscular junction, wherein the signals from nerve to muscle is transferred via the release of Acetylcholine and activate the Acetylcholine receptors.

The nerve is separated from the muscle by a distance of 20 nm and they are held together by a protein filament called **BASAL LAMINA**. The muscle membrane is deeply corrugated and as much as 5 million Acetylcholine receptors are densely packed at the entrance of the cleft.

PRE SYNAPTIC ZONE:

- The pre synaptic zone consists of the distal demyelinated segment of the motor nerve and is ensheathed by Schwann cell attaching the nerve end to the muscle membrane.
- Schwann cells play an important role in regeneration of nerve terminal by releasing the nerve growth factor and neuregulin and cleans the pre synaptic zone by phagocytosis.
- The motor nerve cytoplasm contains numerous synaptic vesicles filled with Acetylcholine and mitochondria.

THE SYNAPTIC CLEFT:

- The synaptic cleft occupies a space of 20 nm between the nerve and the muscle.
- The cleft consists of a basal lamina containing macromolecules that forms an extracellular matrix which aids cell adhesion and approximate neuromuscular signaling process.

- Acetylcholinesterase, alpha and beta isoforms , laminin, agrin are necessary for appropriate neuromuscular transmission.
- Acetylcholine is hydrolyzed by acetlycholinesterase in the synaptic cleft.
- Acetlycholinesterase which is secreted from the muscles is attached to the lamina from where it rapidly breaks down the Acetylcholine.
- In synaptic form of congenital myasthenia syndrome, cholinesterase is low.
- Denervation decreases acetlycholinesterase at the junctional and extrajunctional areas.
- Organophosphate pesticides or nerve gas (eg- sarin) inactivate acetlycholinesterase by phophorylating the serine hydroxyl group located at the active site of acetlycholinesterase.

POST SYNAPTIC ZONE:

- The post synaptic membrane is characterized by numerous folds namely primary folds and secondary folds
- The shallower folds are called as primary and the deeper folds are called as secondary folds.
- Both the folds increases the surface area for neuromuscular transmission.
- Nicotinic Acetylcholine receptors are present in high concentration in the shoulder region and are attached to the cell membrane by cytoskeleton proteins.
- **PERIJUNCTIONAL ZONE** is present closer to the post synaptic membrane.
- The perijunctional zone has a higher density of Sodium channels than the other parts of the cell membrane, making this part of the muscle membrane more capable of amplifying the responses to depolarization and thus to promote the transduction process that finally leads to muscle contraction.

HISTOLOGY OF NEUROMUSCULAR JUNCTION

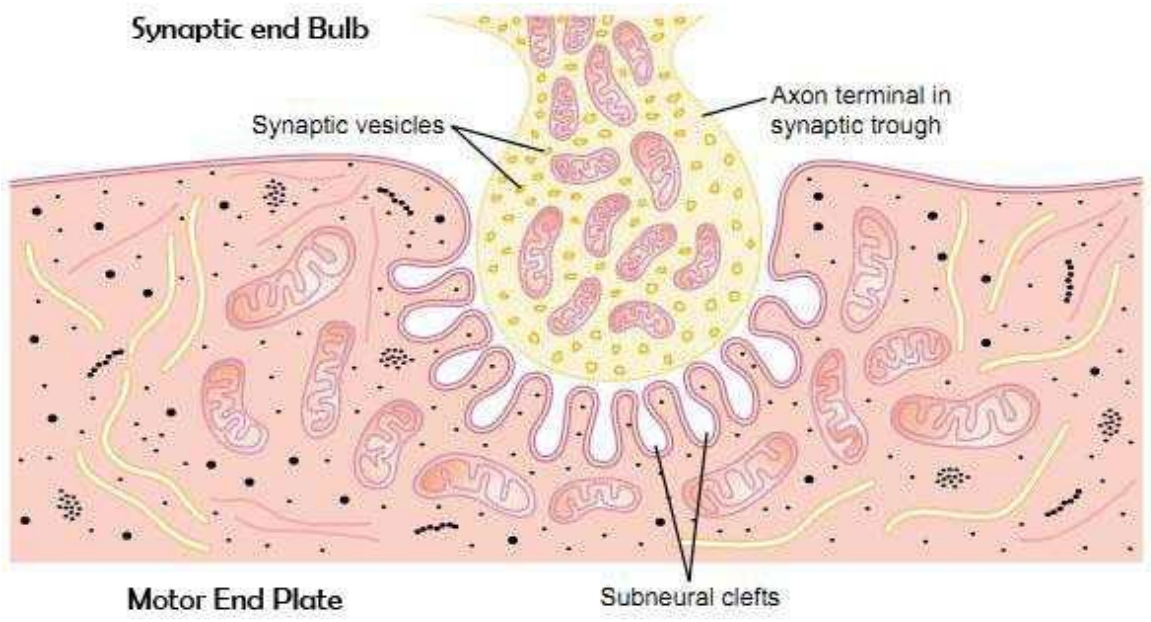

Fig 3.2. MICROSCOPIC VIEW OFNEUROMUSCULAR JUNCTION

The above shows the histological features of neuromuscular junction. It shows the axon terminal in synaptic trough containing synaptic vesicles. These synaptic vesicles are filled with Acetylcholine molecules. It also shows the presence of numerous folds namely the primary and secondary folds. In deeper parts of the fold is the subneural cleft.

STRUCTURE OF ACETYLCHOLINE RECEPTOR:

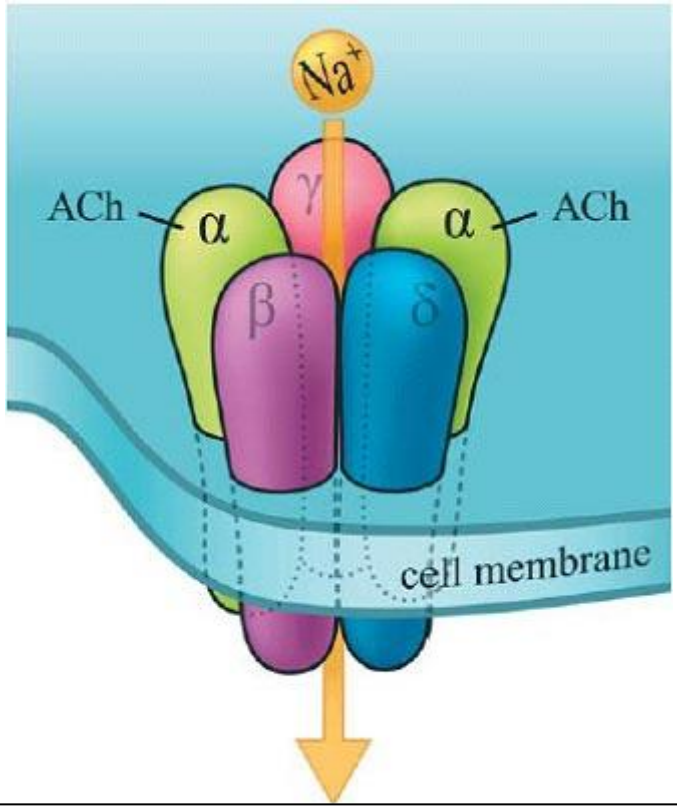

Fig 3.3. STRUCTURE OF ACETYLCHOLINE RECEPTOR

- Each Ach receptor in the neuromuscular junction normally consists of five protein subunits namely 2 alpha and 1 beta, delta and epsilon. Only two identical alpha subunits are capable of binding to Ach molecules.

- If both the alpha binding sites are occupied by Ach molecule, a conformational change in the subunits briefly (1ms) opens an ion channel in the core receptor.
- The channel will not open if Ach is bound to only one alpha site.
- In contrast to normal junctional receptor, another isoform contains a gamma subunit instead of epsilon subunit.
- This isoform is termed as **FETAL or IMMATURE** receptor because initially it is expressed in fetal tissues.
- It is also termed as **EXTRAJUNCTIONAL RECEPTOR** because it is located along the muscle membrane instead of neuromuscular junction.

EXTRA JUNCTIONAL RECEPTORS:

- Just before and shortly after birth and after denervation, the immature gamma containing Acetylcholine receptors are distributed all over the muscle membrane including the motor end plate and they are termed as **EXTRA JUNCTIONAL RECEPTORS**

- Nerve muscle contacts completely matures around 2 years of age.
- Denervation, burns, immobilization, chronic muscle relaxant therapy, stroke, sepsis leads to re-expression of these extra junctional receptors.
- The muscle receptor has a life span of 2 weeks where as the newly developed extra junctional immature gamma Acetylcholine receptors have life span of 24 hours.

PHYSIOLOGY OF NEUROMUSCULAR TRANSMISSION:

- The region of approximation between a motor neuron and a muscle cell is the neuromuscular junction. The cell membranes of the neuron and muscle fibers are separated by a narrow (20 nm) gap namely synaptic cleft.
- As the nerve's action potential depolarizes its terminal, an influx of Calcium ions through voltage-gated Calcium channels into the nerve cytoplasm allows storage vesicles to fuse with the terminal membrane and release their contents of Acetylcholine (Ach).

- The Ach molecules diffuse across the synaptic cleft to bind with nicotinic cholinergic receptors on a specialized portion of the muscle membrane, the motor end plate.
- Each neuromuscular junction contains approximately 5 millions of these receptors.

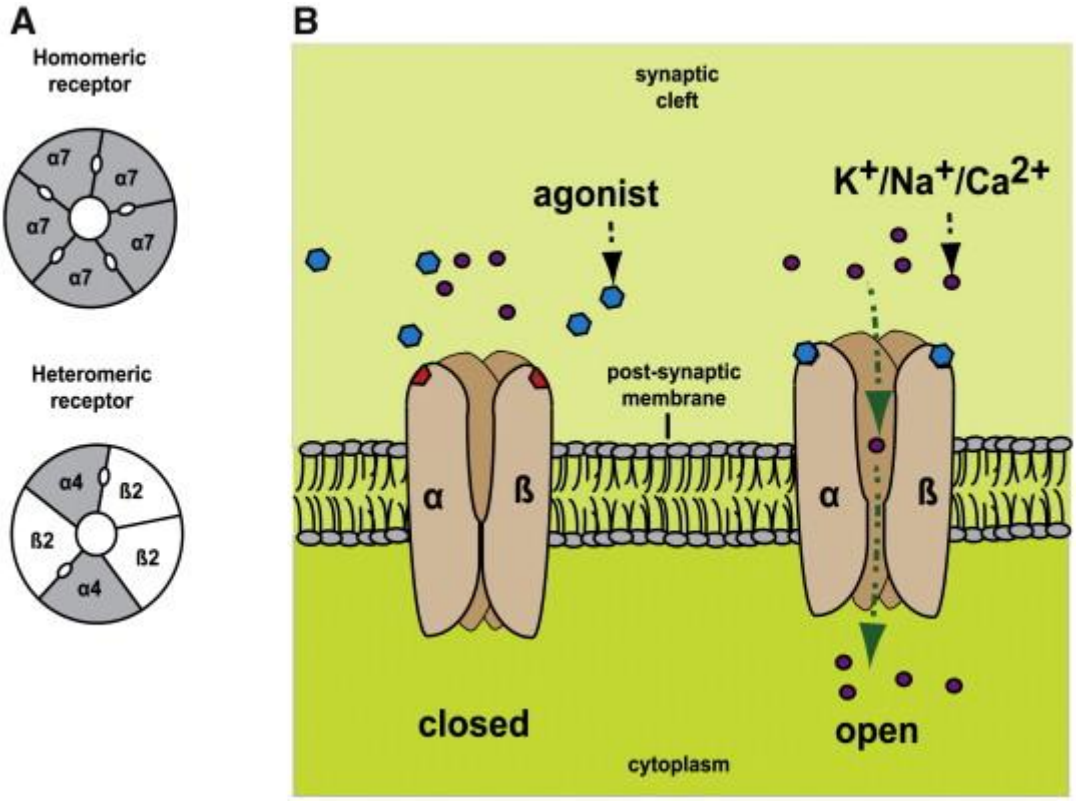

Fig 3.4. SODIUM CHANNEL IN CLOSED & OPEN STATE

The above image demonstrates the series of neuromuscular transmission. It shows the Sodium channel in closed state and open state. When the agonist

bind to the Sodium channel in closed state, the channels opens and influx of Sodium and Calcium ions and efflux of Potassium ions occur generating the action potential.

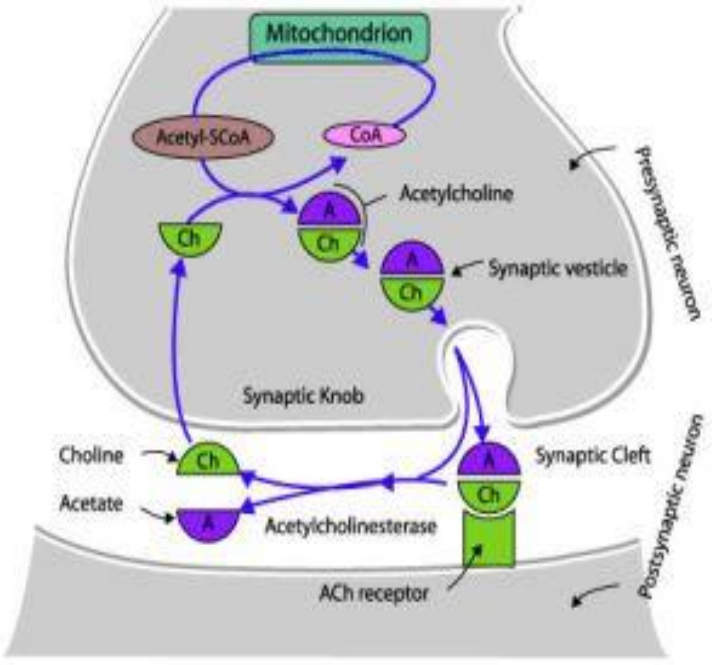

Fig 3.5. CYCLE OF NEUROMUSCULAR TRANSMISSION

- Cations flow through the open Ach receptor channel (Sodium and Calcium in; Potassium out), generating an **END-PLATE POTENTIAL.**
- The contents of a single vesicle, a quantum of Ach (10^4 molecules per quantum), produce a miniature end plate potential.

- The number of quanta released by each nerve impulse, normally at least 200 is very sensitive to extracellular ionized Calcium concentration; increasing Calcium concentration increases the number of quanta released.
- When enough receptors are occupied by Ach, the end-plate potential will be sufficiently strong to depolarize the perijunctional membrane.
- Perijunctional areas of muscle membrane have a high concentration of Sodium channels.
- The generated action potential propagates along the muscle membrane and T-tubule system, which opens the Sodium channels and Calcium from sarcoplasmic reticulum
- This intracellular Calcium facilitates the actin and myosin (contractile proteins) to interact producing muscle contraction.

METABOLISM OF ACETYLCHOLINE

- **ACETYLCHOLINESTERASE** rapidly degrades Acetylcholine into acetate and choline.
- This enzyme is embedded into the motor end plate membrane immediately adjacent to Ach receptors.
- Consequently, the receptor's ion channels close, causing the end plate to repolarize.
- As the generation of action potential ceases, the Sodium channels in the muscle membrane also closes.
- Calcium gets sequestered in the sarcoplasmic reticulum.

PHARMACOLOGY OF SUCCINYLCHOLINE

Succinylcholine is a depolarizing neuromuscular blocker. It is the only clinically available depolarizing muscle relaxant. Structurally it is a two Ach molecules joined together through acetate methyl groups.

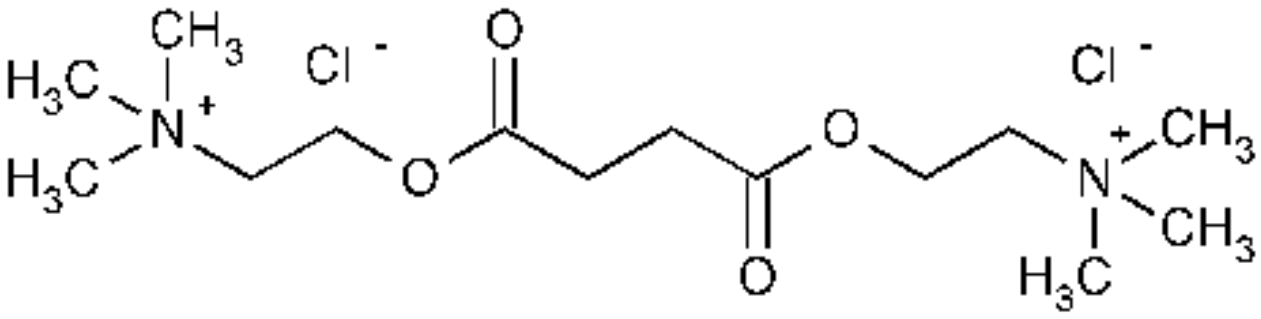

Fig 4.1 STRUCTURE OF ACETYLCHOLINE

MECHANISM OF ACTION

- Succinylcholine structurally resembles Acetylcholine molecule.
- They bind to Ach receptors and generate a muscle action potential.

- Unlike Ach molecule, the Succinylcholine is not metabolized by acetlycholinesterase resulting in their increased concentration in synaptic cleft. This leads to prolonged depolarization of muscle end plate.
- Continuous end plate depolarization causes muscle relaxation because the lower gate in the perijunctional Sodium channels is time limited.
- After initial muscle excitation which is clinically seen as fasciculation, the Sodium channels close and cannot reopen until muscle is repolarized.
- The end plate cannot repolarize until Succinylcholine is bound to Ach receptors. This results in muscle relaxation.

DESENSITIZATION BLOCK

- Desensitization block occurs when Acetylcholine receptors does not undergo any agonistic or conformational change upon stimulation by

Acetylcholine. The receptors become insensitive to agonistic effects of Acetylcholine.

- The mechanism is still unkown.
- Receptor randomly moves from resting to desensitized state constantly.

PHASE II BLOCK

- It is a complex phenomenon that occurs slowly at junction constantly exposed to depolarizing agents.
- Upon repeated opening of channels by constant stimulant action of Acetylcholine, an abnormal electrolyte imbalance occurs that distorts the function of junctional membrane.
- Factors affecting the development of PHASE II BLOCK include duration of exposure, the drug used and the type of muscle itself.

METABOLISM AND EXCRETION:

- The main advantage with Succinylcholine is its rapid onset of action i.e. 30-60 sec and a shorter duration of action namely less than 10 minutes.
- As the drug enters the circulation, it is rapidly metabolized by plasma cholinesterase into Succinylmonocholine.
- This metabolism is so efficient that only a fraction of injected drug reaches the neuromuscular junction to exert its effects.
- Duration of action may be prolonged in high doses or by abnormal metabolism. The causes for abnormal metabolism are hypothermia, low plasma cholinesterase level or genetically different plasma cholinesterase.
- Hypothermia decreases the rate of hydrolysis.
- Low plasma cholinesterase is seen in pregnancy, liver disease, renal failure and interaction with certain drugs.

DOSAGE:

Intravenous route – 1-1.5 mg/kg body weight

PHARMACOLOGICAL EFFECTS OF SUCCINYLCHOLINE

CARDIOVASCULAR EFFECTS

- Because of its resemblance with Acetylcholine molecule, cardiovascular effects are due to stimulation of cholinergic receptors in the heart.
- Cholinergic receptors are present in SA node of heart. By acting at this receptors, Succinylcholine can decrease the rate of sinus impulse generation, and reduce the rate of conduction leading to bradycardia.
- This effect is more pronounced in patients with intrinsically high vagal tone such as paediatric patients and in adults this effect becomes prominent during second dose of Succinylcholine.
- Therefore before repeating the second dose of Succinylcholine, all adult patients must receive an anticholinergic drugs (*e.g.* atropine) to prevent bradycardia.

- Children are more prone for Succinylcholine induced bradycardia than adults. Nodal rhythm or ventricular arrhythmias may develop.

FASCICULATIONS:

- The onset of paralysis by Succinylcholine is usually signaled by fasciculation which are nothing but visible motor unit contractions.
- This muscle fasciculation is responsible for Hyperkalemia, muscle pain, increased intraocular pressure, increased intragastric pressure and increased intracranial pressure.
- **In our study we used Magnesium sulphate to this attenuate fasciculation and its effects.**

MUSCLE PAIN

- Muscle pain (myalgia) commonly presents 24 hours after surgery and it is more severe in ambulatory patients.
- Higher incidence is seen in females, outpatients and large muscular patients. Incidence is less among paediatric, geriatric and pregnant women.
- The pain is thought to be due to unsynchronized muscle contractions and occurs in unusual sites, such as the diaphragm, intercostal muscles and interscapular region.
- There may increase in serum creatine kinase levels following administration of Succinylcholine(indicative of muscle damage).
- Several measures have been tried to reduce the fasciculation such as Rocuronium, Atracurium, Ketorolac, Lignocaine, Diazepam,Magnesium Sulphate, Thiopentone, Diclofenac, small dose of Succicylcholine itself, Vecuronium, Pancuronium, and D-Tubocurare.
- Rocuronium o.06-0.1 mg/kg prior to Scoline has been reported to be effective in preventing fasciculation and myalgia.

HYPERKALEMIA

- Administration of Succinylcholine causes rise in serum K^+ level of around 0.5 – 1.0 mEq/L.
- The reason for rise in serum K^+ is due to Succinylcholine induced muscle fasciculation.
- This rise in serum K^+ level can be life threatening in patients with pre- existing hyperkalemia, burns, massive trauma, neurological disorders.
- This rise in serum K^+ level can lead to cardiac arrhythmias and cardiac arrest.
- This hyperkalemia induced cardiac arrest may be refractory to routine cardiopulmonary resuscitation.

Conditions predisposing to Succinylcholine induced Hyperkalemia:

- Burns
- Massive trauma
- Severe intraabdominal infections
- Spinal cord injury
- Encephalitis
- Stroke

- Guilliane-Barre syndrome
- Severe Parkinson's disease
- Tetanus
- Prolonged immobilization
- Ruptured cerebral aneurysm
- Closed head injury
- Myopathies

MALIGNANT HYPERPYREXIA

- It occurs in susceptible individuals with a congenital abnormality, particularly when it is used with volatile agents like Halothane.
- Heat production exceeds heat loss and there is temperature rise of at least 2^{o} C/ hour.
- It is an inherited autosomal dominant disorder related to the Calcium channels
- It is characterized by following features :
    - Initially spasm of masseter muscle will occur
    - Rapidly rising temperature
    - Cyanosis
    - Mottled skin rashes

- Muscle rigidity in spite of relaxation
- Hyperventilation
- Hypercapnia
- Dysrrhythmias
- Acidosis
- Death due to exhaustion and cardiac failure.

INCREASED INTRA-OCULAR PRESSURE

- The degree of increase in intra-ocular pressure following Succinylcholine 1.0 mg /kg is 4–8 mm Hg.
- The cause of rise in intraocular pressure is due to extraocular muscle contraction. The increase occurs after intravenous injection, peaking at 1–2 min.
- This increase in intraocular pressure may result in expulsion of intraocular contents in patients with penetrating eye injury.

INCREASED INTRAGASTRIC PRESSURE

- Abdominal muscle fasciculation causes Succinylcholine-induced increase in intragastric pressure.
- It never crosses 19 cm H_2O.
- The increase in intragastric pressure is not predictable.
- However, there is no increased risk of aspiration because of corresponding increase in tone of the lower esophageal sphincter , resulting in an increase in barrier pressure.

PHARMACOLOGY OF MAGNESIUM SULPHATE

Magnesium is the second most common intracellular cation after Potassium. Magnesium plays an important role in many enzymatic reactions as a cofactor. It plays an important role in energy metabolism and nucleic acid synthesis. It is also involved in several processes including: hormone receptor binding, gating of Calcium channels, transmembrane ion flux, muscle contraction, neuronal activity, control of vasomotor tone, cardiac excitability and neurotransmitter release.

Magnesium is distributed principally in bone (53%), intracellular compartments of muscle (27%) and soft tissues (19%). Serum Magnesium comprises only 0.3% of total body Magnesium stores. It is present in 3 forms

1. Ionized (62%)
2. Protein bound(33%),mainly albumin
3. Bound to citrate and phosphate (5%)

Magnesium is absorbed in the ileum and colon. Its absorption is inversely proportional to intake. Excretion occurs via the kidney .Along with the other cations Magnesium is filtered at

the glomerulus, but reabsorption occurs in the ascending loop of Henle and not the proximal convoluted tubule.

CHEMICAL STRUCTURE OF MAGNESIUM SULPHATE:

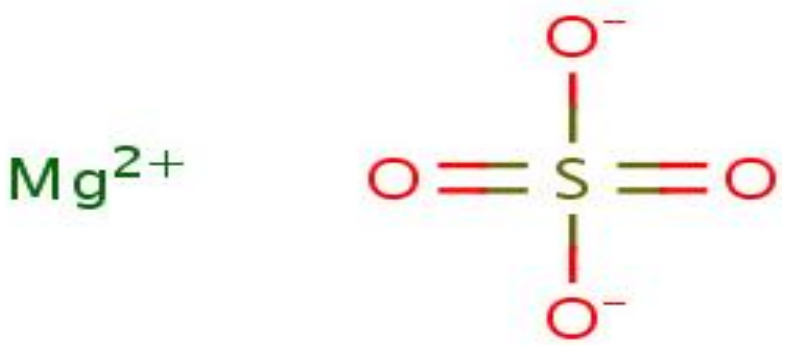

Fig 5.1 STRUCTURE OF MAGNESIUM SULPHATE

Magnesium in its many of its properties mimics a **physiological Calcium antagonist.** A common pathway for the release of hormones, growth factors, and neurotransmitters is phospholipase C activation and hydrolysis to ionositol 4,5 triphosphate (IP_3). This (IP_3) binds to the Calcium channels and releases Calcium. Magnesium is a non-competitive inhibitor of the (IP_3) gated Calcium channel. It may also

inhibit the Ryanodine receptors to release Calcium ions in the sarcoplasmic reticulum.

Only 0.3% of the total body Magnesium is available in serum for estimation. Hence estimation of serum levels does not reflect the total body Magnesium stores. Normal serum Magnesium levels are 1.5 – 2.5 mEq/L. When the levels are below 1.5mEq/L it is called as **HYPOMAGNESEMIA**. When the levels are greater than 2.5mEq/L it is termed as **HYPERMAGNESEMIA**. Another parameter for estimation is 24hr urinary Magnesium concentration which is 5-15 mEq/24hr.

MAGNESIUM DEFICIENCY:

Magnesium deficiency is often multifactorial and is usually found to coexist along with other electrolyte abnormalities, particularly hypokalemia or hypophoshatemia. Following are the causes for Magnesium deficiency (i).reduced intake (ii).poor g.i.absorption (iii) increased loss through diarrhoea, vomiting (iv) increased renal loss (v).diabetes mellitus (vi)

alcoholism (vii) drug induced – diuretics, amino glycosides etc,

Clinical features: (i) usually associated with hypocalcemia and hypokalemia (ii) arrhythmia- Torsades de pointes, a polymorphic ventricular tachycardia (iii) neurologic manifestations include altered mentation, seizures, tremors and hyperreflexia.

A serum concentration of less than 1 mEq/L is treated with 6 g Magnesium sulphate in 250 ml isotonic saline and infused over 3 hours followed by 5 g Magnesium sulphate over next 12 hours. Continue with 5 g Magnesium sulphate every 12 hours for next 5 days. Urine output and respiratory rate are monitored.

MAGNESIUM TOXICITY:

Serum Magnesium levels more than 2.5 mEq/L is termed as **HYPERMAGNESEMIA**.

Following are the causes:

- hemolysis from hemolytic anemia or trauma
- renal insufficiency
- diabetic ketoacidosis
- adrenal insufficiency
- hyperparathyroidism
- Lithium intoxication.

Following are the clinical features:

Manifestation	**Serum Magnesium (mEq/L)**
Hyporeflexia	>4
1 st degree AV block	>5
Complete heart block	>10
Cardiac arrest	>13

MANAGEMENT

- Hemodialysis is the treatment of choice for severe hypermagnesemia
- Intravenous Calcium gluconate 1 g over 2-3 mins is used to antagonise the cardiovascular effects
- Aggressive volume infusion with diuretic like furosemide.

MAGNESIUM SULPHATE IN OBSTETRICS:

- Magnesium sulphate remains the drug of choice in the treatment eclampsia. 4 to 6 gm i.v.
- Magnesium sulphate is diluted in 100 ml of normal saline given over 15 mins. This is followed by infusion of 2 gm/hr i.v. in 100 ml normal saline.
- Target serum Magnesium levels are 4 to 7 mEq/L.
- Another alternative regimen is **Pritchard s** regimen: 4gm Magnesium sulphate given slow i.v. followed by 10 gm, of which 5 g is given in each buttock as deep i.m.injection.

- Use of Magnesium sulphate in cases of pre-eclampsia is yet to be proven.
- Magnesium sulphate is known to have tocolytic effect. An i.v. Bolus of 2-4 g over 24 hrs followed by 1-2 g/hr i .v.infusion and is regulated based on uterine responses.
- Observational studies have proven the decrease in incidence of cerebral palsy in low birth infants in mothers treated with Magnesium sulphate.

MAGNESIUM SULPHATE IN CARDIOLOGY:

- It acts on Calcium channels in the myocardial muscle and also acts

  Indirectly on the cardiac muscle by inhibiting the Calcium uptake on the Troponin C of the myocytes and thereby influencing myocardial contractility.
- Its vasodilatory action is due to its activation of cyclic AMP. This causes reduction in systolic blood pressure.
- Pulmonary vascular resistance is unaltered. Coronary vascular resistance is reduced and causes vasodilation.

Uses:

- In acute Myocardial infarction – 2 gm Magnesium sulphate is administered intravenously over 5 to 15 mins followed by 18 gm over 24 hours.
- In the treatment of arrhythmias-(i) Torsades de pointes intravenously 25 to 50 mg/kg, can be given up to 2 gm.(ii) in atrial or ventricular arrhythmias along with hypokalemia.
- Hypomagnesaemia is common after CABG, hence it is used in postoperative period to prevent arrhythmias.

MAGNESIUM IN NEUROMUSCULAR BLOCK:

- Magnesium ions have an inhibitory effect on postjunctional potentials and decrease in muscle fibre membrane excitability.
- It also has a preponderant action on presynaptic potentials by competitively blocking the entry of Calcium ions.

- Presynaptic inhibition in release of Acetylcholine decreases the effect on postsynaptic receptors which in turn increases the threshold of axonal excitation, thereby potentiating the neuromuscular blockade action.
- By acting as a Calcium antagonist it reduces the Succinylcholine induced muscle fasciculation.

MAGNESIUM IN CENTRAL NERVOUS SYSTEM:

- Magnesium sulphate has been found to possess NMDA receptor antagonistic property thereby inhibits induction and central sensitization after nociceptive stimuli.
- In many studies Magnesium is found to possess the analgesic property when administered intravenous, intrathecal and epidural routes.
- Intravenous dose of magnesium sulphate varies from 30-50mg/kg
- In the neuraxial blockade a dosage of 50 mg has been found to have desired analgesia. Therefore this explains its use in intraoperative and postoperative analgesia.

- Magnesium as already explained possesses anti-epileptic property in Eclampsia, although its effect on other types of seizures is yet to be proved.

MAGNESIUM IN RESPIRATORY SYSTEM:

It has bronchodilatory action is due to

- inhibition of smooth muscle Contraction
- inhibition of histamine release from the mast cells
- inhibition of Acetylcholine release from the cholinergic nerve endings.

Hence it is used in bronchial asthma.

MAGNESIUM DECREASES CATECHOLAMINE RELEASE:

- Magnesium is known to have marked anti adrenergic effect which is mediated by Calcium antagonism.
- This anti-adrenergic property along with vasodilatory and anti-arrhythmic effect makes its use beneficial in Pheochromocytoma.

- This property facilitates its use for nullifying the stress response for tracheal intubation. To reduce the stress response Magnesium sulphate is given in a dose of 30-50 mg/kg.

PREPARATIONS AVAILABLE:

Parenteral injection: Magnesium sulphate- 10%, 12.5%, 50%

For Intravenous use only- 4%, 8%.

- Magnesium sulphate in dextrose: 1% in 5%dextrose & 2%in 5% dextrose. When administered intravenously the onset of action is immediate and duration of action is 30 min.
- On administration by intramuscular route the onset of action takes 1hr and duration of action is 3-4 hrs.
- Storage: 15-30^{o} centigrade. For intravenous use concentration of 20% or less should be used. Rate of injection should be 1.5ml/hr.

DRUG INTERACTIONS:

Central nervous system depressants like Opiates, barbiturates are potentiated by Magnesium sulphate hence dose has to adjusted.

Neuromuscular blocker- they prolong the duration of neuromuscular blockade.

PHARMACOLOGY OF PROPOFOL

Propofol is an intravenous non-barbiturate anaesthetic agent.

Propofol (2,6-diisopropylphenol) consists of a phenol ring with two isopropyl groups attached.

AVAILABLE FORMULATIONS:

- Available as 1% or 2% solution in 10 ml, 20 ml vials. It is not water soluble.
- It is supplied as white oil-in-water emulsion which is relatively thick and oily and so a 20G needle has to be used.
- Originally polyethoxylated castor oil (Cremophor EL) was used for emulsification. Because of anaphylactic reaction caused by this, it has been replaced by 10% soya bean oil, 2.25% glycerol & 1.2% egg phosphatide (lecithin).
- It is painful on injection that can be lessened by prior injection of xylocaine or mixing 2ml of 1% xylocaine 18ml of Propofol.

- As Propofol preparations can support growth of bacteria it is advised to use only ampoules for dispensing and the contents must be used within 6 hours.

PHARMACOKINETICS:

- High lipid solubility results in onset of action that is almost equivalent to one – arm – brain circulation. Due to very short distribution half life awakening from single dose is rapid (2-8 mins).
- The rate of clearance of Propofol exceeds hepatic blood flow because of the presence of extra hepatic metabolism.
- High clearance rate explains rapid recovery after a continuous infusion.
- It has a short initial distribution half life of 2-8 minutes.
- Metabolites of Propofol are excreted in urine. However excretion is not affected in chronic renal failure.

DOSAGE:

Induction dose - 2- 2.5 mg/kg

Maintenance dose – 150-300 microgram/kg/min

Sedation dose - 75-100 microgram/kg/min

CLINICAL EFFECTS:

CARDIOVASCULAR SYSTEM:

- Propofol causes decrease in arterial blood pressure due to a drop in systemic vascular resistance, cardiac contractility and preload.
- It increases the heart rate.
- The relaxation of vascular smooth muscle is due to inhibition of sympathetic vasoconstrictor activity.
- The negative ionotropic effect of Propofol may result from decrease in intracellular Calcium availability secondary to inhibition of trans sarcolemmal Calcium influx.

- Pressor responses to tracheal intubation are reduced compared to Thiopentone.
- It also reduces the hypertensive response to placement of LMA.
- Patients with significant impaired ventricular function may experience a significant drop in cardiac output as a result of decreases in ventricular filling pressures and contractility.
- Profound bradycardia and asystole after administration of Propofol have been described in healthy adult patients despite prophylactic anticholinergics. Treatment may require Isoproterenol.

RESPIRATORY SYSTEM:

- Propofol is a profound respiratory depressant that usually causes apnoea following an induction dose. Opioids may exaggerate this depression of ventilation.
- Propofol infusion inhibits hypoxic ventilatory drive and depresses the normal response to hypercarbia.
- Propofol inhibits the airway reflexes better than Thiopentone.

CEREBRAL EFFECTS:

- Propofol decreases intracranial pressure by decreasing cerebral blood flow.
- In patients with elevated intracranial pressure, Propofol can cause a critical reduction in CPP (cerebral perfusion pressure) to < 50 mm Hg unless steps are taken to support mean arterial pressure.
- Propofol has a unique antipruritic property.
- Since it has antiemetic property, it is preferred in outpatient anaesthesia.
- Induction is accompanied by excitatory phenomena like muscle twitching, spontaneous movements, opisthotonus or hiccupping possibly due to sub cortical glycine antagonism.
- Propofol also has anticonvulsant property and has been successfully used to terminate status epilepticus.
- It also has proconvulsant activity. The majority of Propofol induced seizures during induction of anaesthesia or emergence from anaesthesia reflect spontaneous excitatory movements of sub cortical origin.

HEPATIC AND RENAL FUNCTION:

- Prolonged infusions of Propofol have been associated with hepatocellular injury accompanied by lactic acidosis, bradyarryhmias and rhabdomyolysis.
- Prolonged infusion of Propofol may also result in excretion of green urine reflecting presence of phenols.
- Urinary uric acid excretion may increase and may manifest as cloudy urine.

DRUG INTERACTIONS:

Fentanyl and Alfentanyl concentrations may be increased by concomitant administration of Propofol. Administration of Midazolam along with Propofol has synergistic effect.

ADVERSE EFFECTS:

- Allergic reactions occur due to phenyl nucleus and diisopropyl side chain. It is more common if there is prior sensitization to diisopropyl radical.

➢ PROPOFOL INFUSION SYNDROME –

- It is characterized by lactic acidosis, rhabdomyolysis, and cardiac dysfunction.
- It occurs most often in ICU where prolonged infusion of Propofol is given for sedation
- It occurs when Propofol infusion is given at a dose > 75ug/kg/minute for more than 24 hours.
- It can be suspected when there is unexplained tachycardia during infusion.
- Arterial blood gas analysis and serum lactate levels confirms the diagnosis.

REVIEW OF LITERATURE

1. Mahendra Kumar et al[28]

60 patients were randomized into 2 groups. MG group received 40mg/kg of Magnesium sulphate. NS group received same volume of normal saline. Muscle fasciculation occurred in 50% of patients in MG group and 100% of patients in NS group with a significant p-value of <0.001. After 24 hours surgery, no patient had myalgia in MG group and 30% of patients in NS group had myalgia with a significant p-value of <0.002. They concluded that Magnesium sulphate 40mg/kg intravenously may be used with Propofol for induction of anaesthesia to control Succinylcholine induced fasciculation and myalgia.

2. Danladi KY et al

Eighty-four adult patients undergoing surgery under general endotracheal anaesthesia were randomly allocated into two study groups. Endotracheal intubation was performed with Succinylcholine in group A, while in group B Magnesium

sulphate followed by Succinylcholine. Samples are taken for estimating serum Potassium before induction and at 5 min after induction. Degree of muscle fasciculation and duration of apnea were assessed. This study showed increase in serum Potassium of Group A patients {average 0.34 mmol/L} from baseline with a p value 0.00 which was statistically significant. Magnesium sulphate reduced Succinylcholine - induced hyperkalemia by 0.3 mmol/L (p-value 0.01). The severity of muscle fasciculation was also reduced significantly (p-value 0.00). The duration of apnea during endotracheal intubation (p-value 0.41) was not statistically significant. 14.6% of patients who received Magnesium complained of feeling of heat or warmth. The study showed that Magnesium sulphate administration has significantly reduced Succinylcholine-induced hyperkalemia and severity of muscle fasciculation during induction of general endotracheal anaesthesia. They advocated the use of Magnesium pretreatment in all patients at risk of these complications.

3. Stacey MR et al [16]

Twenty patients were studied in a randomized double-blind manner to evaluate whether Magnesium sulphate, attenuates the side effects caused by Succinylcholine when given during a rapid-sequence induction (RSI). Patients were allocated to two groups in a randomized manner. One group received Magnesium sulphate at a dose of 40mg/kg and the other group received equal volume of normal saline during rapid sequence induction. All the patients were induced with Thiopentone followed by Succinylcholine at a dose of 1.5mg/kg. The level of serum Potassium, the degree of fasciculation and the presence of postoperative myalgia(muscle pain) were recorded. The mean serum Potassium concentration increased by 0.08 mmol/L in the Magnesium sulphate group and by 0.1 mmol/L in the normal saline group at 2 min after injection of Succinylcholine. The hemodynamic parameters like blood pressure and heart rate increased in both groups after endotracheal intubation. The incidence of fasciculations was significantly lower in the Magnesium sulpahte group. Duration of muscle relaxation was not prolonged however. There was no difference between the two groups in the

occurrence of myalgia after surgery (one patient in each group).

4. Sakuraba S et al

did a study to evaluate the effects of Magnesium sulphate and precurarization with Vecuronium on Succinylcholine induced muscle fasciculations.

Fifty-five patients were randomly allocated to three groups by a blinded manner. Group M received Magnesium 40 mg/kg in isotonic saline 100 ml for 5 min at 6.5 min before induction and subsequently administered isotonic saline 1-2 ml at 1.5 min before induction; Group V received isotonic saline 100 ml for 5 min at 6.5 min before induction and subsequently administered Vecuronium 0.02 mg/kg at 1.5 min before induction; Group C received isotonic saline 100 ml for 5 min at 6.5 min before induction and then saline 1-2 ml at 1.5 min before induction. Fasciculation scores and mean changes of heart rate, systolic blood pressure and rate pressure product between baseline and after induction were significantly lower in group M than those in group C and group V. Pretreatment

with Magnesium is more effective in reducing Succinylcholine-induced muscle fasciculation and subsequent tracheal intubation associated hemodynamic changes in rapid sequence induction compared with Vecuronium pretreatment.

5. Tramer MR et al [24]

42 patients undergoing elective abdominal hysterectomy under general anesthesia were randomly allocated into two groups. One group received 20% Magnesium sulfate and other group received isotonic saline (control) 15 ml i.v before the commencement of surgery and infusion at a dose of 2.5 ml/h for the next 20 hours . Postoperative morphine requirement was assessed for 48 h using PCA(patient-controlled analgesia). Maximum expiratory flow (peak flow), pain at rest and during peak flow, and discomfort were evaluated up to the 48th hour in the postoperative period , and 1 week and 1 month after surgery. Insomnia was evaluated after the first and second postoperative nights. Compared to control subjects, Magnesium -treated patients required less morphine during the first 48h ($P<0.03$), and experienced less discomfort during the first and second postoperative days ($P<0.05$-0.005). The

Magnesium -treated group showed no change in postoperative sleeping patterns when compared to preoperative patterns. Control patients showed an increase in insomnia during the first and second postoperative nights ($P<0.002$ and $P<0.005$, respectively) compared to preoperative values. They concluded that perioperative administration of Magnesium sulfate is associated with lesser analgesic requirement, less discomfort, and a better quality of sleep in the postoperative period with no adverse effects.

6. James MF et al [7]

did a study to evaluate role of Magnesium sulphate in reducing Succinylcholine induced changes in serum Potassium concentration. The effect of Magnesium sulfate 60mg/kg on the neuromuscular blockade and subsequent Potassium release produced by 1.5 mg/kg Succinylcholine in ten normal patients was compared with ten patients pretreated with isotonic saline. Magnesium had no significant effect on the duration of muscle relaxation. In control patients, serum Potassium raised by an average of 0.57 +/- 0.20 (SEM) mmol/L. No patient in the Magnesium group had a raise in serum Potassium (mean

change -0.05 +/- 0.02 mmol/L). The difference between the two groups was statistically significant (p value <0.01).

7. Tauzin-Fin P et al [23]

30 ASA I or II patients undergoing radical prostatectomy under general anaesthesia were randomized into 2 groups namely Mg group and control C group. Mg group received Magnesium sulphate at a dose of 50mg/kg diluted in 100 mL of isotonic saline over twenty minutes after induction of anaesthesia and before skin incision. Control group received equal volume of isotonic saline during the same period. At the end of surgery 40 ml of Ropivacaine wound infiltration was given in both the groups. Total requirement of tramadol in Mg group was 224 mg and C group was 446 mg 24 hours after surgery which was statistically significant(p-value of <0.001). They concluded that Magnesium sulphate reduces tramadol consumption.

8. Maddineni VR et al[29]

The incidence and severity of myalgia and change in creatine kinase levels were evaluated following administration of 1 mg/kg of Succinylcholine either immediately or 2 min after induction of anaesthesia with Propofol or Thiopentone in patients undergoing elective dental and ophthalmic surgery. In patients induced with Propofol ,the incidence of myalgia was 35 and 60% when Succinylcholine is given immediately and after 2 min respectively. In patients induced with Thiopentone the incidence of myalgia was 35 and 55% when Succinylcholine is given immediately and after 2 min. There was no statistically significant differences among the groups. Creatine kinase levels increased in both the groups after the operative procedure with the least average increase in the group receiving Succinylcholine immediately after Propofol and the highest increase in the group receiving Succinylcholine 2 min after Thiopentone. There was no statistically significant correlation between the incidence and severity of muscle fasciculations, myalgia and changes in creatine kinase within or between the groups. They concluded that neither the induction agent nor the time between the

induction agent and Succinylcholine administration has any significant influence on the incidence of myalgia or creatine kinase elevation following Succinylcholine.

9. Y.-T. Jeon et al

Sixty one children with Cerebral palsy who underwent orthopedic surgery were randomly divided into 2 groups. The $MgSO_4$ group (Group M) received Magnesium sulphate 0.05g/kg intravenously as a bolus and 0.015 g/kg/h as a continuous infusion throughout the procedure. The saline group (Group S) received equal amount of isotonic saline. Rocuronium was administered at a dose of 600 ug/kg as an intubation dose and 100 ug/kg as a maintenance dose when TOF counts were more than 2. Intravenous Fentanyl and Ketorolac were given for pain relief in the post operative period. Total analgesia consumption and pain scores were evaluated at postoperative thirty minutes, and at 6 hour, 24 hour, and 48 hour. The results obtained in the study was Rocuronium requirement in $MgSO_4$ group (Group M) was significantly less than saline group Group S [0.29 (0.12) *vs* 0.42 (0.16) mg/kg/h, $P<0.05$]. Total analgesic

consumption in $MgSO_4$ group(Group M) was significantly less after surgery at 24 hour and 48 hour with a significant p-value of <0.05, and pain scores in $MgSO_4$ group (Group M) were lower than in saline group(Group S) during the postoperative period with a significant p-value of < 0.05. Serum Magnesium (Mg) concentrations in $MgSO_4$ group (Group M) were higher until 24 hour after surgery with a significant p- value of < 0.05. They concluded that intravenous Magnesium sulphate reduces Rocuronium requirements and postoperative analgesic consumption in children with cerebral palsy.

10. McClymont et al [8]

48 adult female patients undergoing laparoscopic gynaecological surgery were randomly allocated into two groups. One group was induced with Thiopentone and other group was induced with Propofol. The results of their study showed that the incidence of Succinylcholine induced myalgia was low in Propofol group compared to Thiopentone group which was statistically significant with a p-value < 0.05.

MATERIALS AND METHODS

- After approval of the study by our Institutional Ethics Committee, the study was conducted in 60 ASA grade I or II patients undergoing elective surgeries under general anaesthesia.

- The age of the patients ranged from 18– 60 years weighing 50 – 75 kg.

- All patients were thoroughly evaluated preoperatively.

- Informed written consent was obtained and the procedure was explained.

- For all patients age, weight were noted.

- In the preoperative assessment room, vital parameters like pulse rate, blood pressure and baseline investigations like hemoglobin, blood sugar, urea and creatinine, CXR and ECG were checked.

- Thorough examination of all the systems and airway assessment was done.

- Exclusion criteria included patients not fulfilling inclusion criteria, patients with systemic disorders, and patients taking analgesics .

Patients were randomly allocated into 2 groups namely **MG** group and **NS** group

MG GROUP:

Patients received Magnesium sulphate 40mg/kg diluted to 10 ml with distilled water

NS GROUP:

Patients received 0.9% isotonic saline of volume 10 ml.

INCLUSION CRITERIA:

- Age :18 years to 60 years
- ASA : I & II
- Surgery : Elective
- Who have given valid informed consent.

EXCLUSION CRITERIA:

- Not satisfying inclusion criteria.
- Patients with any systemic disease
- Patients taking analgesics

MATERIALS:

- Magnesium suphate 2ml ampoule (0.5g/ml)
- Propofol vial 10ml (10mg/ml)
- Succinylcholine
- Neuromuscular monitoring device
- Monitors – Pulse oximeter, NIBP, ECG
- 2cc and 10cc syringes
- 18 G intravenous cannula, 0.9% normal saline, Ringer lactate

In the operating room, appropriate equipment for airway management and emergency drugs were kept ready. Patients were shifted to the operating room . Non-invasive blood pressure monitor, pulse oximeter and ECG leads were connected to the patient. Preoperative baseline systolic and

diastolic blood pressure, pulse rate and oxygen saturation were recorded. Patients were cannulated with 18 G intravenous cannula . All patients were preloaded with 500 ml of crystalloid solution.

Patients in MS group received Magnesium sulphate 40mg/kg diluted to 10 ml with distilled water over 10 minutes. Whereas patients in NS group received 0.9% isotonic saline of volume 10 ml over 10 minutes. Following which induction is done with Fentanyl 1.5 mcg/kg and Propofol 2mg/kg in both the groups. Then Succinylcholine was administered at a dose of 2mg/kg. Patients were then observed for muscle fasciculations and graded as none, mild, moderate and severe .

PRIMARY OUTCOME MEASURES:

Fasciculations present or not

1. Nil (absent)
2. Mild (fine fasciculations of eyes, face , neck or fingers without movement of limbs)
3. Moderate (obvious muscle twitching at more than one sites or movement of limbs)
4. Severe (vigourous, sustained and widespread fasciculations)

After 24 hours on the next day patients were assessed for postoperative myalgia and graded as none , mild, moderate and severe.

SECONDARY OUTCOME MEASURES:

- Postoperative myalgia after 24 hours
- Grading
    1. Nil (absence of pain)
    2. Mild (muscle stiffness or pain on specific questioning in nape of neck, shoulders and lower chest on deep breathing)
    3. Moderate (muscle stiffness and pain complained of by the patient spontaneously requesting analgesia)
    4. Severe (incapacitating generalized muscle stiffness or pain)

OBSERVATION & ANALYSIS

This prospective randomised double blinded study analyses the effectiveness of Magnesium sulphate in attenuating Succinylcholine induced fasciculation and post op myalgia.

Results are expressed as mean and standard deviation. All the statistical analysis was done using SPSS for Windows version 15.0. The t- test was used for quantitative comparison. Chi square test is used for qualitative comparison. A p-value of less than 0.05 is considered as significant statistically.

60 Patients were taken into the study group, 30 belonged to the group MG and remaining 30 to group NS.

AGE DISTRIBUTION:

	MG Group	**NS Group**
Mean	39.97	39.47
Sd	10.78	12.43
t-Value	**0.17**	
Df	**58**	
p-value	**0.87 (Not Significant)**	

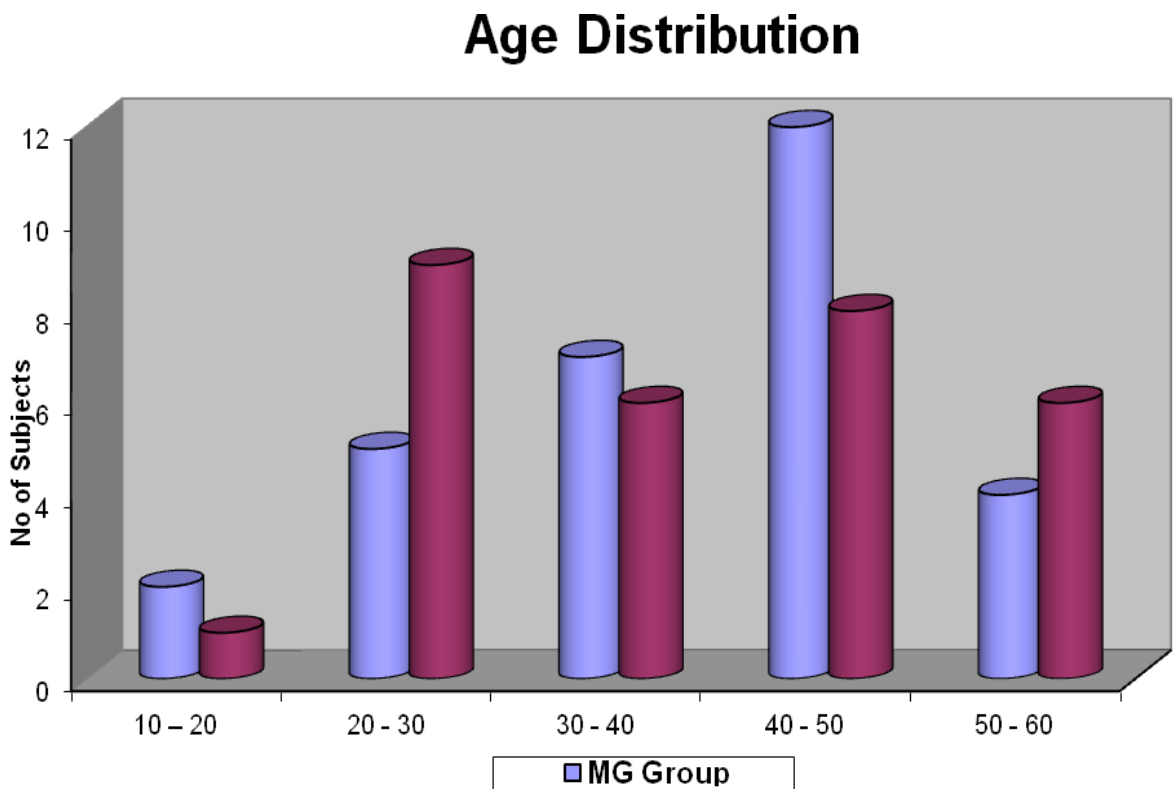

Fig 9.1 GRAPHICAL REPRESENTATION OF AGE DISTRIBUTION

The mean age of group MG is 39.97 and the mean age of group NS is 39.47. From the statistical data , it implies that p-value of Age distribution among NS and MG group is 0.60 which is statistically not significant. Both the groups are comparable in terms of Age.

SEX DISTRIBUTION:

Sex	**MG Group N=30**		**NS Group N=30**		**Total N=60**	
	N	**%**	**N**	**%**	**N**	**%**
Male	25	83.30	23	76.70	48	80.00
Female	5	16.70	7	23.30	12	20.00
Chi-square value	**0.42**					
Df	**1**					
p value	**0.52 (Not Significant)**					

The percentage of male patients in MG group is 83.30% and in NS group is 80%. The percentage of female patients in MG group is 16.70% and in NS group is 20%, p- value is 0.52 which is statistically insignificant. Both the groups are comparable in terms of sex.

WEIGHT DISTRIBUTION:

	MG Group	**NS Group**
Mean	62.30	66.65
Sd	62.30	70.14
t-Value	**0.01**	
Df	**58**	
p-value	**1.00 (Not Significant)**	

The mean weight of the patients in MG group is 62.30 and the mean weight of the patients in NS group is 66.65. The p- value is 1.00 which is statistically insignificant. Both the groups comparable in terms of weight.

ASA PS STATUS:

	MG Group		**NS Group**	
	N	**%**	**N**	**%**
I	22	73.30	20	66.70
II	8	26.70	10	33.30
Total	**30**	**100**	**30**	
Chi square Value *	**0.38**			
Df	**1**			
Significant	**0.57 (Not Significant)**			

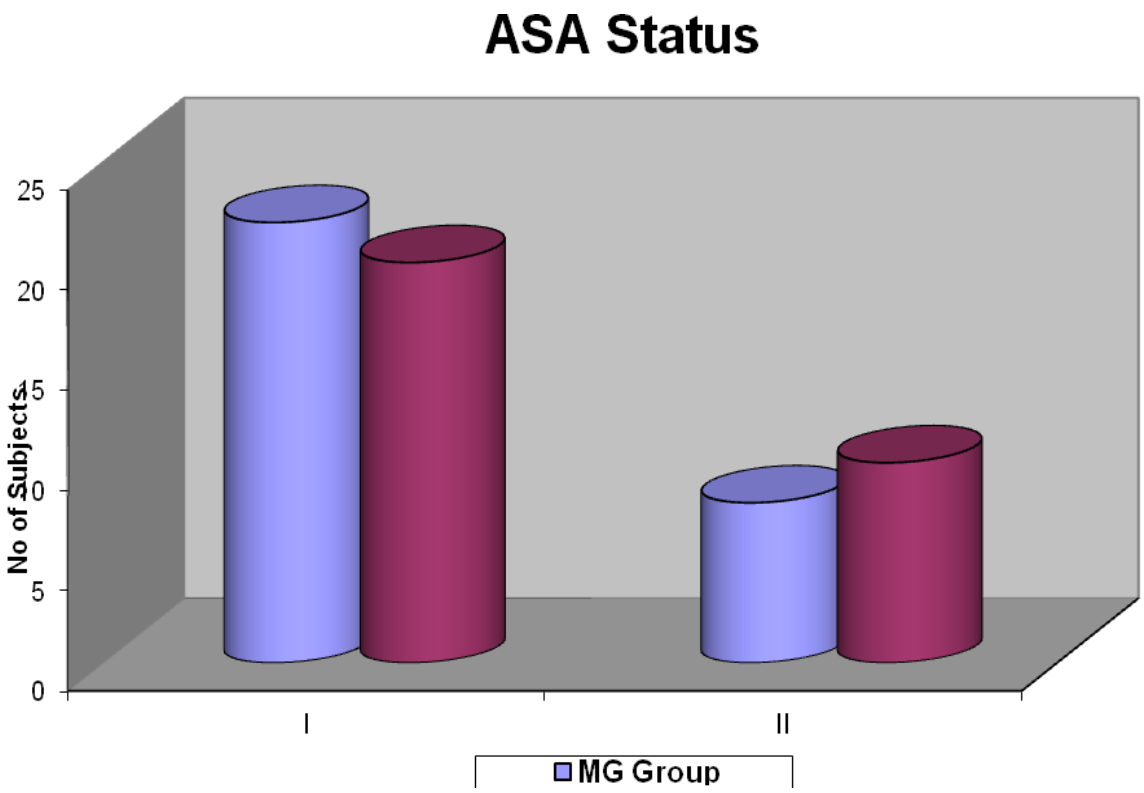

Fig 9.2. GRAPHICAL REPRESENTATION OF ASA PS STATUS

22 patients in MG group and 20 patients in NS group belong to ASA I. 8 patients in MG group and 10 patients in NS group belong to ASA II. p- value is 0.57 which is statistically not significant. Both the groups are comparable in terms of ASA status.

HEART RATE:

Heart Rate	**MG Group** Mean ± sd	**NS Group** Mean ± sd	t-value	p-Value df=58
Base Line	86.90 ± 8.92	89.57 ± 11.70	0.99	0.33*
Before Induction	79.97 ± 8.68	87.67 ± 09.24	3.33	0.002
Post Induction	90.73 ± 7.88	97.43 ± 10.22	2.84	0.01
Post Intubation 1 Mint	100.33 ± 8.47	106.50 ± 11.14	2.41	0.02
Post Intubation 3 Mint	90.73 ± 7.43	95.90 ± 09.52	2.34	0.02
Post Intubation 5 Mint	85.30 ± 6.64	87.37 ± 07.52	1.13	0.26*

* - Not Significant

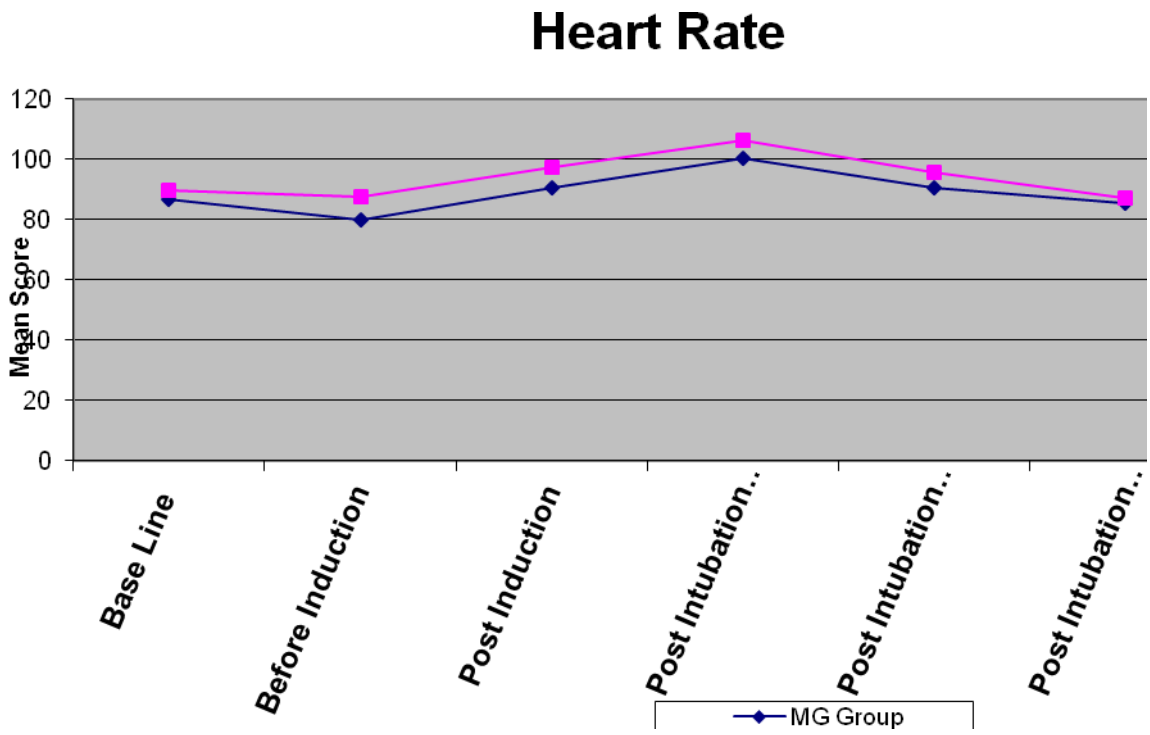

Fig 9.3. GRAPHICAL REPRESENTATION OF HEART RATE

Heart rate is measured at baseline, after giving MgSO4/before induction, post induction, post intubation at 1^{st} , 3^{rd} and 5^{th} minute. Calculated p- values are 0.33, 0.002, 0.01, 0.02, 0.02, 0.26 respectively. Heart rate is statistically significant among the two groups during before induction, post induction, post intubation at 1^{st} and 3^{rd} minute.

SYSTOLIC BLOOD PRESSURE:

Blood Pressure	**MG Group** Mean ± sd	**NS Group** Mean ± sd	t-value	p-Value df=58
Base Line	125.37 ± 8.48	126.83 ± 08.90	0.65	0.52*
Before Induction	121.00 ± 6.87	122.77 ± 06.93	0.99	0.33*
Post Induction	105.10 ± 7.88	103.57 ± 06.37	0.83	0.41*
Post Intubation 1 Mint	113.50 ± 9.41	119.10 ± 20.42	1.36	0.18*
Post Intubation 3 Mint	112.93 ± 9.08	113.60 ± 09.43	0.28	0.78*
Post Intubation 5 Mint	107.73 ± 5.91	107.73 ± 5.91	0.01	1.00*

* - Not Significant

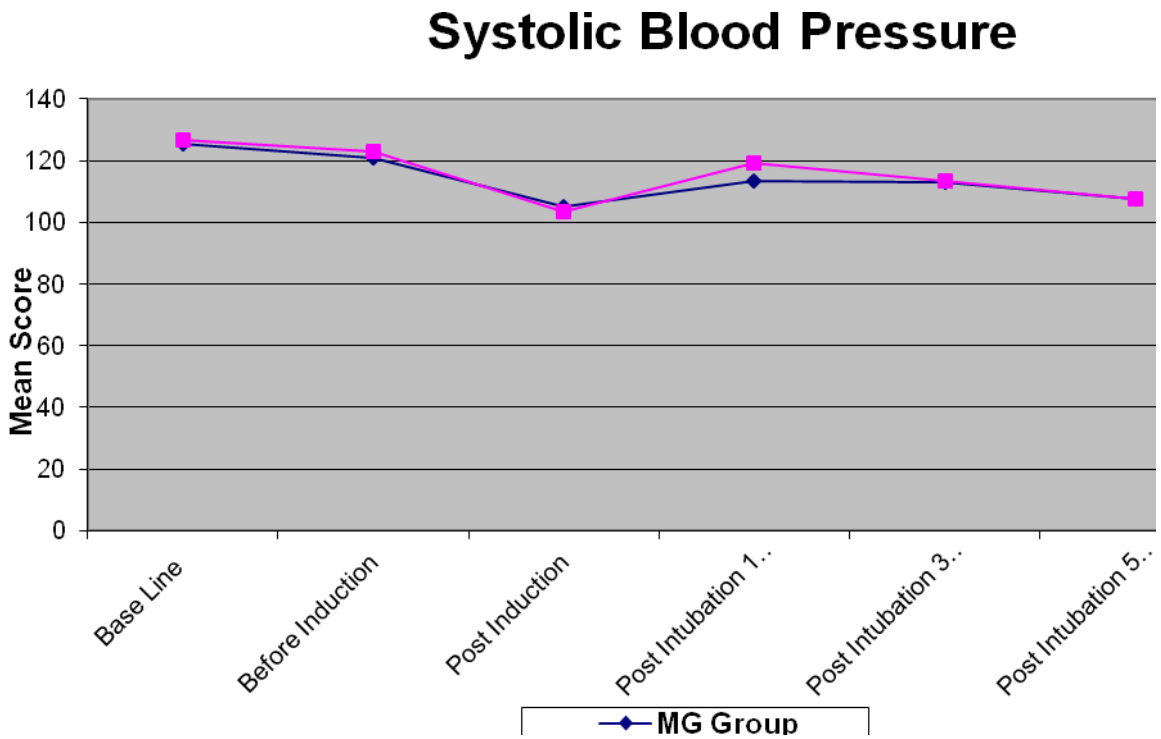

Fig 9.4. GRAPHICAL REPRESENTATION OF SYSTOLIC BLOOD PRESSURE

Systolic blood pressure is measured at baseline, after giving MgSO4/before induction, post induction, post intubation at 1st, 3rd and 5th minute. Calculated p- values are 0.52, 0.33, 0.41, 0.18, 0.78, 1.00 respectively. All the values are statistically not significant.

FASCICULATION:

	MG Group		**NS Group**	
	N	**%**	**N**	**%**
None	15	50.00	0	0
Mild	8	26.70	7	23.30
Moderate	7	23.30	20	66.70
Severe	0	0	3	10.00
Chi square Value *	**24.33**			
Df	**3**			
Significant	**0.0001 (Significant)**			

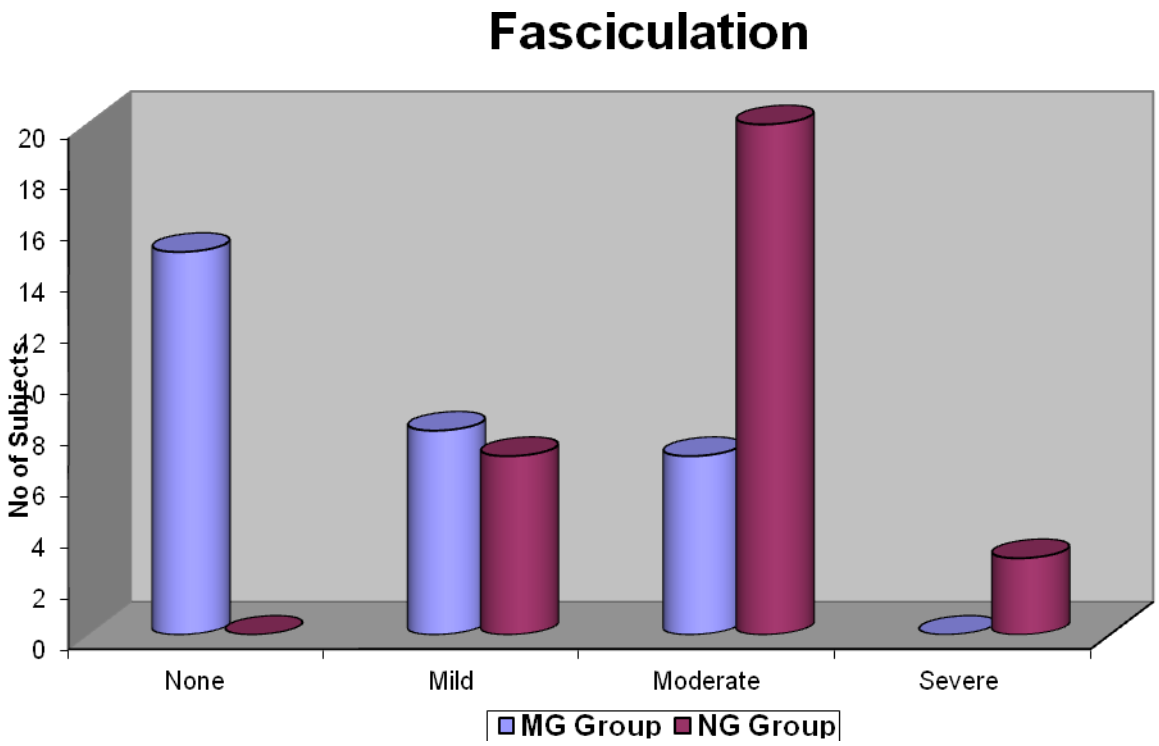

Fig 9.5. GRAPHICAL REPRESENTATION OF FASCICULATION

15 patients had none, 8 had mild, 7 had moderate degree of fasciculation in MG group. 7 patients had mild, 20 had moderate, 3 had severe degree of fasciculation in NS group. p-value is 0.0001 which is statistically significant.

POST OP MYALGIA AFTER 24 HRS

	MG Group		**NS Group**	
	N	**%**	**N**	**%**
None	30	100.00	20	66.70
Mild	0	-	07	23.30
Moderate	0	-	03	10.00
Chi square Value *	**12.00**			
Df	**2**			
Significant	**0.002 (Significant)**			

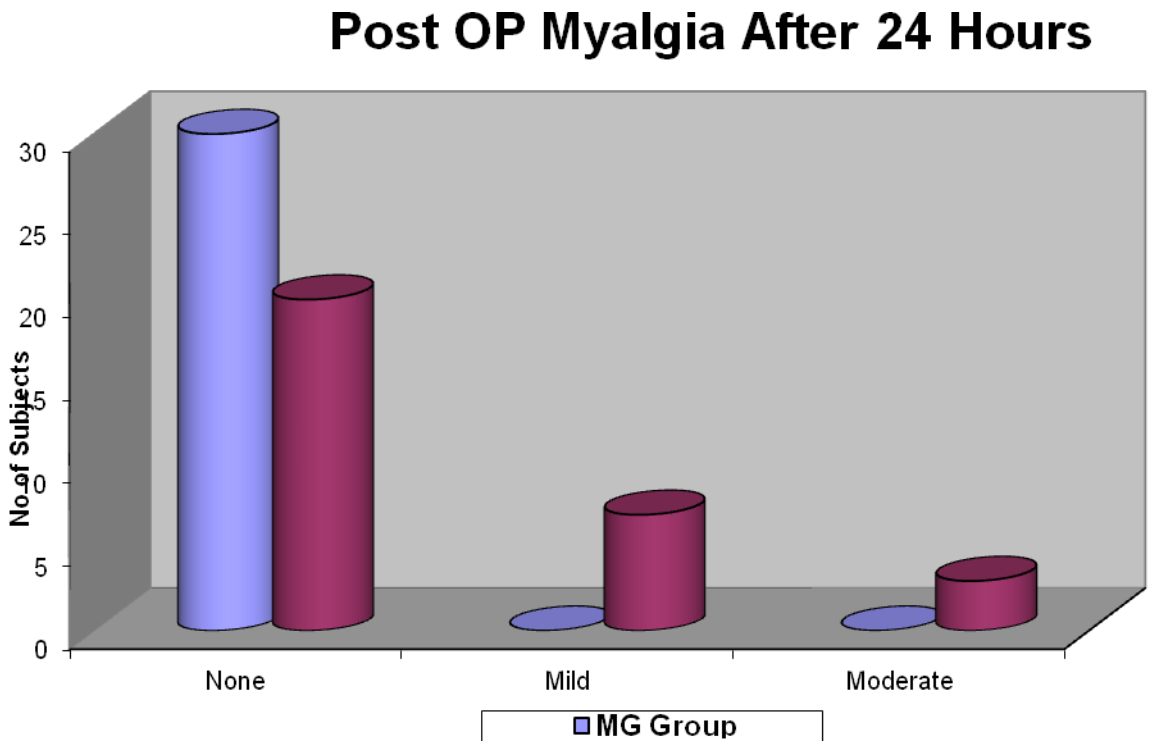

Fig 9.6. GRAPHICAL REPRESENTATION OF POST OPERATIVE MYALGIA AFTER 24 HORS

No patients had post op myalgia in MG group. 7 patients had mild and 3 patients had moderate degree of post op myalgia in NS group. p- value is 0.002 which is statistically significant.

DISCUSSION

Succinylcholine is one of the most commonly used muscle relaxant in clinical practice because of its faster onset, excellent muscle relaxation suitable for intubation and rapid recovery properties.

However use of Succinylcholine is not free of complications namely muscle fasciculation, post operative myalgia, hyperkalemia, increased intraocular pressure and increased intracranial pressure.

Pretreatment with several agents like Rocuronium, Atracurium, Ketorolac, Lignocaine, Diazepam,Magnesium Sulphate, Thiopentone, Diclofenac, small dose Of Succicylcholine itself, Vecuronium, Pancuronium, and D-Tubocurare has been tried in order to reduce the Succinylcholine induced fasciculations and its complications. In our study we used Propofol as an induction agent because it has been found that Propofol is a better agent than Thiopentone in blunting the Succinylcholine induced fasciculations.

1. In our study, the mean age in MG group is 39.97and the mean age in NS group is 39.47 both are comparable in terms of age.

2. The number of male patients in MG group is 25 and in NS group is 23. The number of female patients in MG group is 5 and in NS group is 7. Both are comparable in terms of sex.

3. Mean weight of the patients in MG group is 62.30 and the mean weight of the patients in NS group is 66.65.

4. Number of patients with ASA I in MG group is 22 and in NS group is 20. The number of patients with ASA II in MG group is 8 and in NS group is 10. Both are comparable in terms of ASA PS status.

5. There is significant reduction of heart rate in MG group during before induction, post induction, post intubation at 1^{st} and 3^{rd} minute.

6. In our study 50% of patients in MG group had no fasciculations where as in NS group incidence of fasciculation was 100%.

7. In our study 100% of patients in MG group had no post operative myalgia where as 33.30% patients in NS group had post operative myalgia.

Comparison of our results with study conducted by **Stacey et al**[16] who used Magnesium sulphate 40 mg/kg along with Thiopentone as induction agent shows that 40% of patients had no fasciculation in their study as against 50% in our study. After 24 hours no patients in MG group had myalgia and 9 patients in NS group had myalgia as against on difference in the incidence of myagia compared to our study. The reason for such difference in our study is Propofol is a better agent than Thiopentone in reducing the fasciculations.

Mantaki et al [30] used continuous Propofol infusion for treating Succinylcholine induced post operative myalgia.

Fasciculation produced by Succinylcholine can produce muscle damage resulting in increase in serum creatine kinase

levels and myoglobin level. **Collier et al**[21] observed that in patients who experience Succinylcholine induced post operative myalgia, there is transient fall in serum Ca^{++} levels at 1st minute. They postulated that influx of Calcium into the muscle cells causes the muscle damage and myalgia. At the neuromuscular junction Magnesium has antagonistic action with Calcium. High Magnesium at prejunctional site prevents the release of Acetylcholine from synaptic vesicles where as high Calcium promotes Acetylcholine release. Thus by acting as a Calcium antagonist Magnesium sulpahte blunts the Succinylcholine induced muscle fasciculations.

Jay S. Dr De Vore. M.D. et al[14] (Anaesthesiolgy 52:76-77, 1980) did a study on ten toxemic parturient who were treated with Magnesium sulphate and who eventually underwent cesarean section under general anaesthesia. Magnesium sulphate was given in a dose of 4g in the first hour i.v and then a maintenance dose at a rate of 1g/kg/hr infusion. Anaesthesia was induced with Thiopentone 4mg/kg , followed by Succinylcholine 1.5mg/kg and patients were observed for fasciculations 1min following Succinylcholine. Results obtained were no patients had

muscle fasciculations. The mean serum Magnesium level was 2.9-6.4mg/dl.

We didn't measure serum Magnesium levels in our study. There are studies which used a dose higher than our study and showed no evidence of Magnesium toxicity in their study. **Tramer et al**[24] studied Magnesium levels after giving bolus dose of 3g followed by infusion at a rate of 500mg/hour for 20 hours. The baseline Magnesium level was 0.74 +/- 0.09 mmol/L. The Magnesium levels after 20 hour infusion was 1.34 +/- 0.09 mmol/L with no evidence of hypermagnesimia.

McClymont et al[8] conducted a study in 48 female patients undergoing laparoscopic gynaecological surgeries to study the effect of Succinylcholine induced myalgia. Anaesthesia was induced with either Thiopentone or Propofol . the results were decrease incidence of Succinylcholine induced fasciculation in patients induced with Propofol(19%) than patients induced with Thiopentone(63%) with a significant p-value <0.05.

SUMMARY

From this prospective randomized double blinded study which evaluated the effect of Magnesium sulphate in attenuating Succinylcholine induced muscle fasciculation and post operative myalgia, we found that,

1. The demographic profiles like Age, Sex, weight , ASA PS status are comparable in both the groups.

2. There was 50% reduction in the incidence of muscle fasciculation in the group pretreated with Magnesium sulphate whereas the incidence of fasciculation was 100% in the control group.

3. The incidence of post operative Succinylcholine induced myalgia was **0%** in group pretreated with Magnesium sulphate whereas there was **33.30%** incidence of post operative myalgia in control group.

CONCLUSION

From our study we conclude that **MAGNESIUM SULPHATE** at a dose of 40mg/kg effectively reduces the Succinylcholine induced muscle fasciculation and Succinylcholine induced post operative myalgia.

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PROFORMA

DATE: ROLL NO: Drug used:

NAME:

AGE: IPNO: SEX:

DIAGNOSIS:

SURGICAL PROCEDURE DONE:

PRE OP ASSESSMENT:

HISTORY: Any Co-morbid illness

Any

H/O previous surgeries

MEASURES OF STUDY OUTCOME:

	HR	SPO2	SBP
BASELINE BEFORE MgSO4			
BEFORE INDUCTION			
POST IINDUCTION			

POST INTUBATION

1 MIN:

3 MIN:

5 MIN:

FASCICULATION:

NONE MILD MODERATE SEVERE

POST OP MYALGIA AFTER 24 HOURS

NONE MILD MODERATE SEVERE